IL-17C drives skin inflammation in calcipotriol-induced rodent model of atopic dermatitis

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Introduction

Interleukin-17C (IL-17C) is a distinct member of the IL-17-family that has been shown to play a central pro-inflammatory role in psoriasis1,2. MOR106 is a human IgG1 monoclonal antibody that potently and selectively binds to human and mouse IL-17C, thereby inhibiting the binding of IL-17C to its IL-17RE receptor. This inhibition of biological activity in vitro translated into in vivo efficacy as this antibody was shown to suppress the development of experimental psoriasis in the IL-23-driven murine skin inflammation model.

Objective

We hypothesized that IL-17C as a local amplifier of skin inflammation, could also play a role in other inflammatory skin diseases beyond psoriasis. Here we started to explore the role of IL-17C in the development of atopic dermatitis.

Methods

- Expression of IL-17C was analysed by IHC using biotinylated MOR22420 antibody in human AD skin lesions
- The effect of MOR106 on development of AD-like syndrome was assessed in the calcipotriol-induced cutaneous inflammation model of atopic dermatitis essentially according to Li et al.

- IL-17C neutralization attenuates calcipotriol-induced skin inflammation and AD-like syndrome

- Statistical analysis was performed with a one-way analysis of variance (ANOVA) and Dunnett post hoc test versus calcipotriol isotype Ab control. *p<0.05; **p<0.01; ***p<0.001

Conclusions

- IL-17C expression is highly upregulated in human AD lesional skin. Expression was increased in keratinocytes and was also detected in infiltrating immune cells in the dermis.
- Blocking function of IL-17C with MOR106 reduces the development of AD-like skin inflammation and associated cutaneous responses in the calcipotriol-induced AD mouse model.
- Inhibiting IL-17C activity is a potential novel therapeutic paradigm for treating AD. MOR106 is currently evaluated in a Phase 1 study in patients with AD (NCT02739009).

IL-17C expression is increased in lesional skin of AD patients

IL-17C neutralization attenuates calcipotriol-induced skin inflammation and AD-like syndrome

References